

Application Ser. No.: 10/613,588

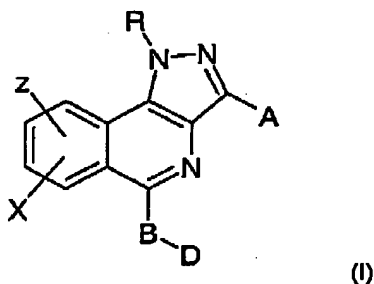
Filing Date: July 03, 2003

Examiner: Desai, Rita

Amendment Pursuant to 37 C.F.R. § 1.121**IN THE CLAIMS:**

The claims set forth below with amendments as indicated will replace all prior versions and listing of claims in the application.

1. (currently amended) A compound of the formula I



or a stereoisomeric form or a pharmaceutically acceptable salt of the compound of the formula I, wherein

A is -(C₁-C₆)-alkyl, in which alkyl is straight-chain or branched and is optionally substituted, once or more, independently of each other, by

-O-R¹ or

-C(O)-OR¹,

-C(O)-NR¹R¹,

-C(O)-NR¹-SO₂R¹,

-NR¹R¹,

-CN, in which R¹ is

hydrogen,

-(C₁-C₆)-alkyl,

-(C₆-C₁₄)aryl or

fluoroalkyl of the formula -C_nH_xF_y or fluoroalkoxy of

the formula -OC_nH_xF_y, wherein n is an integer from 1

to 6, x is an integer from 0 to 12, y is an integer from

1 to 13 and sum of x and y is 2n + 1,

-O-R¹,

-SR¹,

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-S(O)-R¹

-S(O)₂-R¹

-C(O)-OR¹,

fluoroalkyl of the formula -C_nH_xF_y or fluoroalkoxy of the formula

-OC_nH_xF_y, wherein n is an integer from 1 to 6, x is an integer from 0 to 12, y is an integer from 1 to 13 and sum of x and y is 2n + 1,

-C(O)-NR¹R¹,

-C(O)-NR¹-SO₂R¹,

-NR¹R¹,

-CN,

monocyclic or polycyclic heteroaryl having from 5 to 14 ring members, which contains 1 to 5 heteroatoms as ring members, wherein heteroatoms are selected from N, O and S, and in which heteroaryl is unsubstituted or optionally substituted once or more, independently of each other, by R², in which R² is

-(C₁-C₄)-alkyl,

-OH,

-O-(C₁-C₄)-alkyl,

halogen,

-N(R³)-R⁴, in which R³ and R⁴ are, independently of each other, hydrogen atom or -(C₁-C₄)-alkyl,

fluoroalkyl of the formula -C_nH_xF_y or fluoroalkoxy of the formula -OC_nH_xF_y, wherein n is an integer from 1 to 4, x is an integer from 0 to 8, y is an integer from 1 to 9 and sum of x and y is 2n + 1,

-CN,

-SR¹,

-S(O)-R¹,

-S(O)₂-R¹ or

-C(O)-NR¹R¹,

-(C₃-C₆)-cycloalkyl, in which cycloalkyl is unsubstituted or substituted, once or more, independently of each other, by R², and R² is defined as above,

monocyclic or bicyclic heterocycle having from 5 to 12 ring members, which contains 1 to 5 heteroatoms as ring members, wherein

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heteroatoms are selected from N, O and S, and in which heterocycle is unsubstituted or substituted, once or more, independently of each other, by R^2 , and R^2 is defined as above,

B is a covalent bond,

$-C=CR^1-$,

$-C\equiv C-$

$-O(CH_2)_a-$, in which a is an integer from 1 to 4,
O, S, NR^2 , $-C(O)-$, $-NR^2-C(O)-$, $-C(O)-NR^2-$, $-NR^2-SO_2-$,
 $-SO_2-NR^2-$, $-NR^2-C(O)-NR^2-$, and R^2 is defined as above, or
 $-(C_1-C_4)$ -alkylene, in which alkylene is straight-chain or
branched and is optionally substituted, once or more,
independently of each other, by R^1 , and R^1 is defined as
above,

D is $-(C_1-C_6)$ -alkyl, in which alkyl is straight-chain or branched
and is optionally substituted, once or more, independently of each
other, by R^1 , and R^1 is defined as above,

monocyclic or polycyclic heteroaryl having from 5 to 14 ring
members, which contains 1 to 5 heteroatoms as ring
members, and in which heteroaryl is unsubstituted or is
substituted once or more, independently of each other, by
 R^2 , and R^2 is defined as above,

monocyclic or bicyclic heterocycle having from 5 to 12 ring
members, which contains 1 to 5 heteroatoms as ring
members, and in which heterocycle is unsubstituted or
substituted, once or more, independently of each other, by
 R^2 , and R^2 is defined as above,

$-(C_6-C_{14})$ -aryl, in which aryl is unsubstituted or substituted,
once or more, independently of each other, by R^2 , and R^2 is
defined as above, or

$-(C_3-C_8)$ -cycloalkyl, in which cycloalkyl is unsubstituted or
substituted, once or more, independently of each other, by
 R^2 , and R^2 is defined as above, or

B-D is hydrogen,
halogen,

fluoroalkyl of the formula $-C_nH_xF_y$ or fluoroalkoxy of the
formula $-OC_nH_xF_y$, wherein n is an integer from 1 to 4, x is

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an integer from 0 to 8, y is an integer from 1 to 9 and sum of x and y is $2n + 1$,

$-(CH_2)_a-Y-R^3$, in which a is an integer from 1 to 4, Y is O, S, NR^2 , and R^3 is

$-(C_1-C_6)$ -alkyl,

$-(C_6-C_{14})$ -aryl,

$-(C_3-C_8)$ -cycloalkyl, and

R is hydrogen,
 $-(C_1-C_6)$ -alkyl, or
 $-(C_6-C_{14})$ -aryl- $-(C_1-C_6)$ -alkyl, in which aryl is unsubstituted or substituted, once or more, independently of each other, by R^2 , and R^2 is defined as above, and

X and Z are identical or different and are, independently of each other selected from:

hydrogen atom,

$-(C_1-C_4)$ -alkyl,

-OH,

-O- $-(C_1-C_4)$ -alkyl),

halogen,

fluoroalkyl of the formula $-C_nH_xF_y$ or fluoroalkoxy of the formula $-OC_nH_xF_y$, wherein n is an integer from 1 to 6, x is an integer from 0 to 12, y is an integer from 1 to 13 and sum of x and y is $2n + 1$,

$-C(O)-OR^1$,

$-C(O)-NR^1R^1$,

$-C(O)-NR^1-SO_2R^1$,

$-NR^1R^1$,

$-NR^1-C(O)-NR^1R^1$,

$-NR^1-C(O)-R^1$,

$-NR^1-C(O)-OR^1$,

$-O-C(O)-NR^1R^1$,

-CN,

$-SR^1$,

$-S(O)-R^1$,

$-S(O)_2-R^1$,

$-S(O)_2-NR^1R^1$,

$-NR^1-SO_2-R^1$, in which R^1 is as defined above,

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monocyclic or bicyclic heterocycle having from 5 to 12 ring members, which contains 1 to 5 heteroatoms as ring members, wherein heteroatoms are selected from N, O and S, and in which heterocycle is unsubstituted or substituted, once or more, independently of each other, by R^2 , and R^2 is defined as above, or

-(C₃-C₆)-cycloalkyl, in which cycloalkyl is unsubstituted or substituted, once or more, independently of each other, by R^2 , and R^2 is defined as above,

with the proviso that when A is -(C₁-C₆)-alkyl, in which alkyl is straight-chain or branched and is optionally substituted, once or more, independently of each other, by

-O- R^1 or

-C(O)-OR¹, in which R^1 is

hydrogen,

-(C₁-C₆)-alkyl,

-O- R^1 , in which R^1 is as defined in this proviso,

-C(O)-OR¹, in which R^1 is as defined in this proviso, or

monocyclic or polycyclic heteroaryl having from 5 to 14 ring members, which contains 1 to 5 heteroatoms as ring members, wherein heteroatoms are selected from N, O and S, and in which heteroaryl is unsubstituted or optionally substituted once or more, independently of each other, by R^2 , in which R^2 is

hydrogen,

-(C₁-C₄)-alkyl,

-OH,

-O-(C₁-C₄)-alkyl,

halogen, or

-N(R^3)- R^4 , in which R^3 and R^4 are, independently of each other, hydrogen atom or -(C₁-C₄)-alkyl, then:

B is not a covalent bond or -(C₁-C₄)-alkylene.

2. (original) A compound of the formula I as claimed in claim 1, wherein

A is -(C₁-C₃)-alkyl, in which alkyl is straight-chain or branched and is optionally substituted, once or more, independently of each other, by

-O- R^1 , or

-C(O)-OR¹, in which R^1 is

hydrogen,

-(C₁-C₃)-alkyl, or

-CF₃

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fluoroalkyl of the formula $-C_nH_xF_y$ or fluoroalkoxy of the formula $-OC_nH_xF_y$, wherein n is an integer from 1 to 3, x is an integer from 0 to 6, y is an integer from 1 to 7 and sum of x and y is $2n + 1$,

B is a covalent bond or O,

D is phenyl or naphthyl, in which phenyl or naphthyl is unsubstituted or substituted, once or more, independently of each other, by R^2 , in which R^2 is

fluorine, chlorine or bromine,

-OH,

-CF₃,

-SR¹, in which R¹ is defined as above,

-(C₁-C₄)-alkyl

-O-(C₁-C₂)-alkyl or

-N(R³)-R⁴, in which R³ and R⁴ are, independently of each other, hydrogen atom or -(C₁-C₃)-alkyl,

heteroaryl selected from the group consisting of pyridyl, furanyl, pyrrolyl, isoxazolyl, benzofuranyl, benzothiophenyl, quinoliny, isoquinoliny, quinoxaliny and thiophenyl, in which heteroaryl is unsubstituted or substituted, once or more, independently of each other, by R^2 , in which R^2 is defined as above or

-(C₄-C₈)-cycloalkyl, in which cycloalkyl is unsubstituted or substituted, once or more, independently of each other, by R^2 , and R^2 is defined as above, or

B-D is $((CH_2)_a-Y-R^3)$, in which a is an integer from 1 to 2, Y is O and R³ is -(C₁-C₃)-alkyl, and

R is hydrogen,

-(C₁-C₃)-alkyl, or

-phenyl-(C₁-C₃)-alkyl, and

X and Z are identical or different and are, independently of each other, hydrogen, -C(O)-O(C₁-C₃)-alkyl, -OCH₃, -N(CH₃)₂ or halogen.

3. (original) A compound of the formula 1 as claimed in claim 1, wherein the compound of the formula I is selected from the group consisting of:
- 5-pyridin-2-yl-3-trifluoromethyl-1H-pyrazolo[4,3-c]isoquinoline,
 - 3-methyl-5-(2-trifluoromethyl-phenyl)-1H-pyrazolo[4,3-c]isoquinoline,
 - 3-methyl-5-(3-trifluoromethyl-phenyl)-1H-pyrazolo[4,3-c]isoquinoline,

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3-methyl-5-(4-trifluoromethyl-phenyl)-1H-pyrazolo[4,3-c]isoquinoline,
1,3-dimethyl-5-(3-trifluoromethylphenyl)-1H-pyrazolo[4,3-c]-isoquinoline,
5-phenyl-3-trifluoromethyl-1H-pyrazolo[4,3-c]isoquinoline,
1,3-dimethyl-5-(3-trifluoromethylphenyl)-1H-pyrazolo[4,3-c]-isoquinoline,
1,3-dimethyl-5-(2,6-difluorophenyl)-1H-pyrazolo[4,3-c]-isoquinoline,
1-benzyl-5-cyclohexyl-3-methyl-1H-pyrazolo[4,3-c]-isoquinoline,
1-benzyl-5-naphthyl-3-methyl-1H-pyrazolo[4,3-c]-isoquinoline,
5-methoxymethyl-3-methyl-1H-pyrazolo[4,3-c]-isoquinoline,
7-methoxycarbonyl-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]-isoquinoline,
7-methoxycarbonyl-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-
isoquinoline,
7-dimethylamino-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]isoquinoline,
7-dimethylamino-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-isoquinoline,
6-dimethylamino-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]isoquinoline,
6-dimethylamino-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-isoquinoline,
8-dimethylamino-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]isoquinoline,
8-dimethylamino-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-isoquinoline,
1,3-dimethyl-5-(3-methyl-thiophen-2-yl)-1H-pyrazolo[4,3-c]-isoquinoline,
3-methyl-5-phenyl-9-trifluoromethyl-1H-pyrazolo[4,3-c]isoquinoline,
3-methyl-5-pyridin-2-yl-9-trifluoromethyl-1H-pyrazolo[4,3-c]-isoquinoline,
and
3-methyl-5-(2,3,4,5,6-pentafluoro-phenyl)-1H-pyrazolo[4,3-c]-isoquinoline.

4. (canceled)

5. (original) A pharmaceutical composition comprising a therapeutically effective content of at least one compound of the formula I as claimed in claim 1 together with a pharmaceutically suitable carrier optionally in combination with a suitable additive, other active compounds and auxiliary substances.

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6. (original) A method of treating a disease condition associated with the increased activity of NIK comprising administering to a patient suffering from said disease condition a therapeutically effective amount of a compound according to claim 1.
7. (original) The method as claimed in claim 6, wherein the compound is according to claim 2.
8. (original) The method as claimed in claim 6 wherein said compound is selected from the group consisting of:
- 5-pyridin-2-yl-3-trifluoromethyl-1H-pyrazolo[4,3-c]isoquinoline,
3-methyl-5-(2-trifluoromethyl-phenyl)-1H-pyrazolo[4,3-c]isoquinoline,
3-methyl-5-(3-trifluoromethyl-phenyl)-1H-pyrazolo[4,3-c]isoquinoline,
3-methyl-5-(4-trifluoromethyl-phenyl)-1H-pyrazolo[4,3-c]isoquinoline,
1,3-dimethyl-5-(3-trifluoromethylphenyl)-1H-pyrazolo[4,3-c]-isoquinoline,
5-phenyl-3-trifluoromethyl-1H-pyrazolo[4,3-c]isoquinoline,
1,3-dimethyl-5-(3-trifluoromethylphenyl)-1H-pyrazolo[4,3-c]-isoquinoline,
1,3-dimethyl-5-(2,6-difluorophenyl)-1H-pyrazolo[4,3-c]-isoquinoline,
1-benzyl-5-cyclohexyl-3-methyl-1H-pyrazolo[4,3-c]-isoquinoline,
1-benzyl-5-naphthyl-3-methyl-1H-pyrazolo[4,3-c]-isoquinoline,
5-methoxymethyl-3-methyl-1H-pyrazolo[4,3-c]-isoquinoline,
7-methoxycarbonyl-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]-isoquinoline,
7-methoxycarbonyl-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-isoquinoline,
7-dimethylamino-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]isoquinoline,
7-dimethylamino-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-isoquinoline,
1,3-dimethyl-5-(3-methyl-thiophen-2-yl)-1H-pyrazolo[4,3-c]-isoquinoline,
3-methyl-5-phenyl-9-trifluoromethyl-1H-pyrazolo[4,3-c]isoquinoline,
3-methyl-5-pyridin-2-yl-9-trifluoromethyl-1H-pyrazolo[4,3-c]-isoquinoline,
and

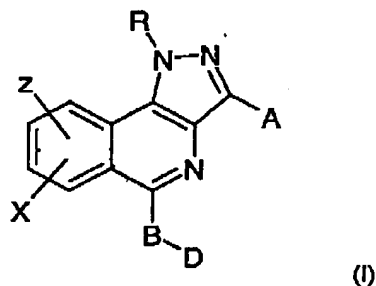
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3-methyl-5-(2,3,4,5,6-pentafluoro-phenyl)-1H-pyrazolo[4,3-c]-isoquinoline.

9. (original) The method as claimed in claim 6, wherein the disease condition is caused due to an inflammatory component.
10. (original) The method as claimed in claim 6, wherein the diseases are osteoarthritis, rheumatoid arthritis, asthma, irritable bowel disease, Alzheimer's disease, stroke, diabetes, atherosclerosis, multiple sclerosis, rejection reactions on the part of the body against a transplanted organ or rejection reactions on the part of the transplanted organ against the body.
11. (currently amended) A pharmaceutical composition comprising a compound of the formula (I)



or a stereoisomeric form or a pharmaceutically acceptable salt of the compound of the formula I, wherein

A is $-(C_1-C_6)$ -alkyl, in which alkyl is straight-chain or branched and is optionally substituted, once or more, independently of each other, by

$-O-R^1$ or
 $-C(O)-OR^1$,
 $-C(O)-NR^1R^1$,
 $-C(O)-NR^1-SO_2R^1$,

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-NR¹R¹,

-CN, in which R¹ is

hydrogen,

-(C₁-C₆)-alkyl,

-(C₆-C₁₄)aryl or

fluoroalkyl of the formula -C_nH_xF_y or fluoroalkoxy of

the formula -OC_nH_xF_y, wherein n is an integer from 1

to 6, x is an integer from 0 to 12, y is an integer from

1 to 13 and sum of x and y is 2n + 1,

-O-R¹,

-SR¹,

-S(O)-R¹

-S(O)₂-R¹

-C(O)-OR¹,

fluoroalkyl of the formula -C_nH_xF_y or fluoroalkoxy of the

formula -OC_nH_xF_y, wherein n is an integer from 1 to 6, x is

an integer from 0 to 12, y is an integer from 1 to 13 and sum

of x and y is 2n + 1,

-C(O)-NR¹R¹,

-C(O)-NR¹-SO₂R¹,

-NR¹R¹,

-CN,

monocyclic or polycyclic heteroaryl having from 5 to 14 ring

members, which contains 1 to 5 heteroatoms as ring

members, wherein heteroatoms are selected from N, O and

S, and in which heteroaryl is unsubstituted or optionally

substituted once or more, independently of each other, by

R², In which R² is

-(C₁-C₄)-alkyl,

-OH,

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-O-(C₁-C₄)-alkyl,

halogen,

-N(R³)-R⁴, in which R³ and R⁴ are, independently of each other, hydrogen atom or -(C₁-C₄)-alkyl,

fluoroalkyl of the formula -C_nH_xF_y or fluoroalkoxy of the formula -OC_nH_xF_y, wherein n is an integer from 1 to 4, x is an integer from 0 to 8, y is an integer from 1 to 9 and sum of x and y is 2n + 1,

-CN,

-SR¹,

-S(O)-R¹,

-S(O)₂-R¹ or

-C(O)-NR¹R¹,

-(C₃-C₆)-cycloalkyl, in which cycloalkyl is unsubstituted or substituted, once or more, independently of each other, by R², and R² is defined as above,

monocyclic or bicyclic heterocycle having from 5 to 12 ring members, which contains 1 to 5 heteroatoms as ring members, wherein heteroatoms are selected from N, O and S, and in which heterocycle is unsubstituted or substituted, once or more, independently of each other, by R², and R² is defined as above,

B is a covalent bond,

-C=CR¹-,

—C≡C—

-O(CH₂)_a-, in which a is an integer from 1 to 4,

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O, S, NR^2 , $-\text{C}(\text{O})-$, $-\text{NR}^2-\text{C}(\text{O})-$, $-\text{C}(\text{O})-\text{NR}^2-$, $-\text{NR}^2-\text{SO}_2-$, $-\text{SO}_2-\text{NR}^2-$, $-\text{NR}^2-\text{C}(\text{O})-\text{NR}^2-$, and R^2 is defined as above, or $-(\text{C}_1-\text{C}_4)$ -alkylene, in which alkylene is straight-chain or branched and is optionally substituted, once or more, independently of each other, by R^1 , and R^1 is defined as above,

D is $-(\text{C}_1-\text{C}_6)$ -alkyl, in which alkyl is straight-chain or branched and is optionally substituted, once or more, independently of each other, by R^1 , and R^1 is defined as above,

monocyclic or polycyclic heteroaryl having from 5 to 14 ring members, which contains 1 to 5 heteroatoms as ring members, wherein heteroatoms are selected from N, O and S, and in which heteroaryl is unsubstituted or is substituted once or more, independently of each other, by R^2 , and R^2 is defined as above,

monocyclic or bicyclic heterocycle having from 5 to 12 ring members, which contains 1 to 5 heteroatoms as ring members, wherein heteroatoms are selected from N, O and S, and in which heterocycle is unsubstituted or substituted, once or more, independently of each other, by R^2 , and R^2 is defined as above,

$-(\text{C}_6-\text{C}_{14})$ -aryl, in which aryl is unsubstituted or substituted, once or more, independently of each other, by R^2 , and R^2 is defined as above, or

$-(\text{C}_3-\text{C}_6)$ -cycloalkyl, in which cycloalkyl is unsubstituted or substituted, once or more, independently of each other, by R^2 , and R^2 is defined as above, or

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B-D is hydrogen,
halogen,

fluoroalkyl of the formula $-C_nH_xF_y$ or fluoroalkoxy of the formula $-OC_nH_xF_y$, wherein n is an integer from 1 to 4, x is an integer from 0 to 8, y is an integer from 1 to 9 and sum of x and y is $2n + 1$,

$-(CH_2)_a-Y-R^3$, in which a is an integer from 1 to 4, Y is O, S, NR^2 , and R^3 is

$-(C_1-C_6)$ -alkyl,
 $-(C_6-C_{14})$ -aryl,
 $-(C_3-C_6)$ -cycloalkyl, and

R is hydrogen,
 $-(C_1-C_6)$ -alkyl, or
 $-(C_6-C_{14})$ -aryl- (C_1-C_6) -alkyl, in which aryl is unsubstituted or substituted, once or more, independently of each other, by R^2 , and R^2 is defined as above, and

X and Z are identical or different and are, independently of each other selected from:

hydrogen atom,
 $-(C_1-C_4)$ -alkyl,
-OH,
-O- (C_1-C_4) -alkyl),
halogen,
fluoroalkyl of the formula $-C_nH_xF_y$ or fluoroalkoxy of the formula $-OC_nH_xF_y$, wherein n is an integer from 1 to 6, x is an integer from 0 to 12, y is an integer from 1 to 13 and sum of x and y is $2n + 1$,
 $-C(O)-OR^1$,
 $-C(O)-NR^1R^1$,

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-C(O)-NR¹-SO₂R¹,
-NR¹R¹,
-NR¹-C(O)-NR¹R¹,
-NR¹-C(O)-R¹,
-NR¹-C(O)-OR¹,
-O-C(O)-NR¹R¹,
-CN,
-SR¹,
-S(O)-R¹,
-S(O)₂-R¹,
-S(O)₂-NR¹R¹,
-NR¹-SO₂-R¹, in which R¹ is as defined above,

monocyclic or bicyclic heterocycle having from 5 to 12 ring members, which contains 1 to 5 heteroatoms as ring members, wherein heteroatoms are selected from N, O and S, and in which heterocycle is unsubstituted or substituted, once or more, independently of each other, by R², and R² is defined as above, or

-(C₃-C₈)-cycloalkyl, in which cycloalkyl is unsubstituted or substituted, once or more, independently of each other, by R², and R² is defined as above,

with the proviso that when A is -(C₁-C₆)-alkyl, in which alkyl is straight-chain or branched and is optionally substituted, once or more, independently of each other, by

-O-R¹ or
-C(O)-OR¹, in which R¹ is
hydrogen,
-(C₁-C₆)-alkyl,
-O-R¹, in which R¹ is as defined in this proviso,
-C(O)-OR¹, in which R¹ is as defined in this proviso, or

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monocyclic or polycyclic heteroaryl having from 5 to 14 ring members, which contains 1 to 5 heteroatoms as ring members, wherein heteroatoms are selected from N, O and S, and in which heteroaryl is unsubstituted or optionally substituted once or more, independently of each other, by R^2 , in which R^2 is

hydrogen,
-(C₁-C₄)-alkyl,
-OH,
-O-(C₁-C₄)-alkyl,
halogen, or

-N(R³)-R⁴, in which R³ and R⁴ are, independently of each other, hydrogen atom or -(C₁-C₄)-alkyl, then:

B is not a covalent bond or -(C₁-C₄)-alkylene.

12. (original) The composition as claimed in claim 11, wherein

A is -(C₁-C₃)-alkyl, in which alkyl is straight-chain or branched and is optionally substituted, once or more, independently of each other, by

-O-R¹, or
-C(O)-OR¹, in which R¹ is
hydrogen,
-(C₁-C₃)-alkyl, or
-CF₃

fluoroalkyl of the formula -C_nH_xF_y or fluoroalkoxy of the formula -OC_nH_xF_y, wherein n is an integer from 1 to 3, x is an integer from 0 to 6, y is an integer from 1 to 7 and sum of x and y is 2n + 1,

B is a covalent bond or O,

D is phenyl or naphthyl, in which phenyl or naphthyl is unsubstituted or substituted, once or more, independently of each other, by R^2 , in which R^2 is

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fluorine, chlorine or bromine,
-OH,
-CF₃,
-SR¹, in which R¹ is defined as above,
-(C₁-C₄)-alkyl
-O-(C₁-C₂)-alkyl or
-N(R³)-R⁴, in which R³ and R⁴ are, independently of each other, hydrogen atom or -(C₁-C₃)-alkyl,

heteroaryl selected from the group consisting of pyridyl, furanyl, pyrrolyl, isoxazolyl, benzofuranyl, benzothiophenyl, quinoliny, isoquinoliny, quinoxaliny and thiophenyl, in which heteroaryl is unsubstituted or substituted, once or more, independently of each other, by R², in which R² is defined as above or

-(C₄-C₆)-cycloalkyl, in which cycloalkyl is unsubstituted or substituted, once or more, independently of each other, by R², and R² is defined as above, or

B-D is ((CH₂)_a-Y-R³, in which a is an integer from 1 to 2, Y is O and R³ is -(C₁-C₃)-alkyl, and

R is hydrogen,

-(C₁-C₃)-alkyl, or
-phenyl-(C₁-C₃)-alkyl, and

X and Z are identical or different and are, independently of each other, hydrogen, -C(O)-O(C₁-C₃)alkyl, -OCH₃, -N(CH₃)₂ or halogen.

13. (original) The composition as claimed in claim 11, wherein the compound of the formula I is selected from the group consisting of:

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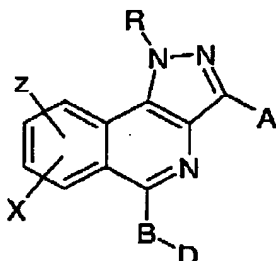
5-pyridin-2-yl-3-trifluoromethyl-1H-pyrazolo[4,3-c]isoquinoline,
3-methyl-5-(2-trifluoromethyl-phenyl)-1H-pyrazolo[4,3-c]isoquinoline,
3-methyl-5-(3-trifluoromethyl-phenyl)-1H-pyrazolo[4,3-c]isoquinoline,
3-methyl-5-(4-trifluoromethyl-phenyl)-1H-pyrazolo[4,3-c]isoquinoline,
1,3-dimethyl-5-(3-trifluoromethylphenyl)-1H-pyrazolo[4,3-c]-isoquinoline,
5-phenyl-3-trifluoromethyl-1H-pyrazolo[4,3-c]isoquinoline,
1,3-dimethyl-5-(3-trifluoromethylphenyl)-1H-pyrazolo[4,3-c]-isoquinoline,
1,3-dimethyl-5-(2,6-difluorophenyl)-1H-pyrazolo[4,3-c]-isoquinoline,
1-benzyl-5-cyclohexyl-3-methyl-1H-pyrazolo[4,3-c]-isoquinoline,
1-benzyl-5-naphthyl-3-methyl-1H-pyrazolo[4,3-c]-isoquinoline,
5-methoxymethyl-3-methyl-1H-pyrazolo[4,3-c]-isoquinoline,
7-methoxycarbonyl-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]-isoquinoline,
7-methoxycarbonyl-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-
isoquinoline,
7-dimethylamino-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]isoquinoline,
7-dimethylamino-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-isoquinoline,
6-dimethylamino-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]isoquinoline,
6-dimethylamino-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-isoquinoline,
8-dimethylamino-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]isoquinoline,
8-dimethylamino-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-isoquinoline,
1,3-dimethyl-5-(3-methyl-thiophen-2-yl)-1H-pyrazolo[4,3-c]-isoquinoline,
3-methyl-5-phenyl-9-trifluoromethyl-1H-pyrazolo[4,3-c]isoquinoline,
3-methyl-5-pyridin-2-yl-9-trifluoromethyl-1H-pyrazolo[4,3-c]-isoquinoline,
and
3-methyl-5-(2,3,4,5,6-pentafluoro-phenyl)-1H-pyrazolo[4,3-c]-isoquinoline.

14. (currently amended) A method of treating a disease condition associated with inflammation comprising administering to a patient suffering from said disease condition a therapeutically effective amount of a compound of formula (I):

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(I)

or a stereoisomeric form or a pharmaceutically acceptable salt of the compound of the formula I, wherein

A is $-(C_1-C_6)$ -alkyl, in which alkyl is straight-chain or branched and is optionally substituted, once or more, independently of each other, by

$-O-R^1$ or

$-C(O)-OR^1$,

$-C(O)-NR^1R^1$,

$-C(O)-NR^1-SO_2R^1$,

$-NR^1R^1$,

$-CN$, in which R^1 is

hydrogen,

$-(C_1-C_6)$ -alkyl,

$-(C_6-C_{14})$ aryl or

fluoroalkyl of the formula $-C_nH_xF_y$ or fluoroalkoxy of

the formula $-OC_nH_xF_y$, wherein n is an integer from 1 to 6, x

is an integer from 0 to 12, y is an integer from 1 to 13 and

sum of x and y is $2n + 1$,

$-O-R^1$,

$-SR^1$,

$-S(O)-R^1$

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-S(O)₂-R¹

-C(O)-OR¹,

fluoroalkyl of the formula -C_nH_xF_y or fluoroalkoxy of the formula -OC_nH_xF_y, wherein n is an integer from 1 to 6, x is an integer from 0 to 12, y is an integer from 1 to 13 and sum of x and y is 2n + 1,

-C(O)-NR¹R¹,

-C(O)-NR¹-SO₂R¹,

-NR¹R¹,

-CN,

monocyclic or polycyclic heteroaryl having from 5 to 14 ring members, which contains 1 to 5 heteroatoms as ring members, wherein heteroatoms are selected from N, O and S, and in which heteroaryl is unsubstituted or optionally substituted once or more, independently of each other, by

R², in which R² is

-(C₁-C₄)-alkyl,

-OH,

-O-(C₁-C₄)-alkyl,

halogen,

-N(R³)-R⁴, in which R³ and R⁴ are, independently of each other, hydrogen atom or -(C₁-C₄)-alkyl,

fluoroalkyl of the formula -C_nH_xF_y or fluoroalkoxy of the formula -OC_nH_xF_y, wherein n is an integer from 1 to 4, x is an integer from 0 to 8, y is an integer from 1 to 9 and sum of x and y is 2n + 1,

-CN,

-SR¹,

-S(O)-R¹,

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$-\text{S}(\text{O})_2-\text{R}^1$ or

$-\text{C}(\text{O})-\text{NR}^1\text{R}^1$,

$-(\text{C}_3-\text{C}_6)\text{-cycloalkyl}$, in which cycloalkyl is unsubstituted or substituted, once or more, independently of each other, by R^2 , and R^2 is defined as above,

monocyclic or bicyclic heterocycle having from 5 to 12 ring members, which contains 1 to 5 heteroatoms as ring members, wherein heteroatoms are selected from N, O and S, and in which heterocycle is unsubstituted or substituted, once or more, independently of each other, by R^2 , and R^2 is defined as above,

B is a covalent bond,

$-\text{C}=\text{CR}^1-$,

$-\text{C}\equiv\text{C}-$,

$-\text{O}(\text{CH}_2)_a-$, in which a is an integer from 1 to 4,

O, S, NR^2 , $-\text{C}(\text{O})-$, $-\text{NR}^2-\text{C}(\text{O})-$, $-\text{C}(\text{O})-\text{NR}^2-$, $-\text{NR}^2-\text{SO}_2-$, $-\text{SO}_2-\text{NR}^2-$, $-\text{NR}^2-\text{C}(\text{O})-\text{NR}^2-$, and R^2 is defined as above, or

$-(\text{C}_1-\text{C}_4)\text{-alkylene}$, in which alkylene is straight-chain or branched and is optionally substituted, once or more, independently of each other, by R^1 , and R^1 is defined as above,

D is $-(\text{C}_1-\text{C}_6)\text{-alkyl}$, in which alkyl is straight-chain or branched and is optionally substituted, once or more, independently of each other, by R^1 , and R^1 is defined as above,

monocyclic or polycyclic heteroaryl having from 5 to 14 ring members, which contains 1 to 5 heteroatoms as ring members, wherein heteroatoms are selected from N, O and S, and in which

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heteroaryl is unsubstituted or is substituted once or more,
independently of each other, by R^2 , and R^2 is defined as above,

monocyclic or bicyclic heterocycle having from 5 to 12 ring
members, which contains 1 to 5 heteroatoms as ring members,
wherein heteroatoms are selected from N, O and S, and in which
heterocycle is unsubstituted or substituted, once or more,
independently of each other, by R^2 , and R^2 is defined as above,

-(C_6 - C_{14})-aryl, in which aryl is unsubstituted or substituted,
once or more, independently of each other, by R^2 , and R^2 is defined
as above, or

-(C_3 - C_6)-cycloalkyl, in which cycloalkyl is unsubstituted or
substituted, once or more, independently of each other, by R^2 , and R^2
is defined as above, or

B-D is hydrogen,
halogen,

fluoroalkyl of the formula $-C_nH_xF_y$ or fluoroalkoxy of the
formula $-OC_nH_xF_y$, wherein n is an integer from 1 to 4, x is an integer
from 0 to 8, y is an integer from 1 to 9 and sum of x and y is $2n + 1$,

$-(CH_2)_a-Y-R^3$, in which a is an integer from 1 to 4, Y is O, S, NR^2 , and
 R^3 is

-(C_1 - C_6)-alkyl,
-(C_6 - C_{14})-aryl,
-(C_3 - C_6)-cycloalkyl, and

R is hydrogen,

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-(C₁-C₆)-alkyl, or
-(C₆-C₁₄)-aryl-(C₁-C₆)-alkyl, in which aryl is unsubstituted or substituted, once or more, independently of each other, by R², and R² is defined as above, and

X and Z are identical or different and are, independently of each other selected from:

hydrogen atom,
-(C₁-C₄)-alkyl,
-OH,
-O-(C₁-C₄-alkyl),
halogen,
fluoroalkyl of the formula -C_nH_xF_y or fluoroalkoxy of the formula -OC_nH_xF_y, wherein n is an integer from 1 to 6, x is an integer from 0 to 12, y is an integer from 1 to 13 and sum of x and y is 2n + 1,
-C(O)-OR¹,
-C(O)-NR¹R¹,
-C(O)-NR¹-SO₂R¹,
-NR¹R¹,
-NR¹-C(O)-NR¹R¹,
-NR¹-C(O)-R¹,
-NR¹-C(O)-OR¹,
-O-C(O)-NR¹R¹,
-CN,
-SR¹,
-S(O)-R¹,
-S(O)₂-R¹,
-S(O)₂-NR¹R¹,
-NR¹-SO₂-R¹, in which R¹ is as defined above,

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monocyclic or bicyclic heterocycle having from 5 to 12 ring members, which contains 1 to 5 heteroatoms as ring members, wherein heteroatoms are selected from N, O and S, and in which heterocycle is unsubstituted or substituted, once or more, independently of each other, by R², and R² is defined as above, or

-(C₃-C₆)-cycloalkyl, in which cycloalkyl is unsubstituted or substituted, once or more, independently of each other, by R², and R² is defined as above,

with the proviso that when A is -(C₁-C₆)-alkyl, in which alkyl is straight-chain or branched and is optionally substituted, once or more, independently of each other, by

-O-R¹ or

-C(O)-OR¹, in which R¹ is hydrogen,

-(C₁-C₆)-alkyl,

-O-R¹, in which R¹ is as defined in this proviso,

-C(O)-OR¹, in which R¹ is as defined in this proviso, or

monocyclic or polycyclic heteroaryl having from 5 to 14 ring members, which contains 1 to 5 heteroatoms as ring members, wherein heteroatoms are selected from N, O and S, and in which heteroaryl is unsubstituted or optionally substituted once or more, independently of each other, by R², in which R² is

hydrogen,

-(C₁-C₄)-alkyl,

-OH,

-O-(C₁-C₄)-alkyl,

halogen, or

-N(R³)-R⁴, in which R³ and R⁴ are, independently of each other, hydrogen atom or -(C₁-C₄)-alkyl, then

B is not a covalent bond or -(C₁-C₄)-alkylene.

15. (original) The method as claimed in claim 14 wherein

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A is $-(C_1-C_3)$ -alkyl, in which alkyl is straight-chain or branched and is optionally substituted, once or more, independently of each other, by

$-O-R^1$, or

$-C(O)-OR^1$, in which R^1 is

hydrogen,

$-(C_1-C_3)$ -alkyl, or

$-CF_3$

fluoroalkyl of the formula $-C_nH_xF_y$ or fluoroalkoxy of the formula $-OC_nH_xF_y$, wherein n is an integer from 1 to 3, x is an integer from 0 to 6, y is an integer from 1 to 7 and sum of x and y is $2n + 1$.

B is a covalent bond or O,

D is phenyl or naphthyl, in which phenyl or naphthyl is unsubstituted or substituted, once or more, independently of each other, by R^2 , in which R^2 is

fluorine, chlorine or bromine,

$-OH$,

$-CF_3$,

$-SR^1$, in which R^1 is defined as above,

$-(C_1-C_4)$ -alkyl

$-O-(C_1-C_2)$ -alkyl or

$-N(R^3)-R^4$, in which R^3 and R^4 are, independently of each other, hydrogen atom or $-(C_1-C_3)$ -alkyl,

heteroaryl selected from the group consisting of pyridyl, furanyl, pyrrolyl, isoxazolyl, benzofuranyl, benzothiophenyl, quinollinyl, isoquinolinyl, quinoxalinyl and thiophenyl, in which

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heteroaryl is unsubstituted or substituted, once or more,
independently of each other, by R^2 , in which R^2 is defined as above or

$-(C_4-C_6)$ -cycloalkyl, in which cycloalkyl is
unsubstituted or substituted, once or more, independently of each
other, by R^2 , and R^2 is defined as above, or

B-D is $((CH_2)_a-Y-R^3$, in which a is an integer from 1 to 2, Y is O and R^3
is $-(C_1-C_3)$ -alkyl, and

R is hydrogen,

$-(C_1-C_3)$ -alkyl, or
-phenyl- (C_1-C_3) -alkyl, and

X and Z are identical or different and are, independently of each other,
hydrogen, $-C(O)-O(C_1-C_3)alkyl$, $-OCH_3$, $-N(CH_3)_2$ or halogen.

16. (original) The method as claimed in claim 14, wherein the compound of
formula (I) is selected from the group consisting of:

5-pyridin-2-yl-3-trifluoromethyl-1H-pyrazolo[4,3-c]isoquinoline,
3-methyl-5-(2-trifluoromethyl-phenyl)-1H-pyrazolo[4,3-c]isoquinoline,
3-methyl-5-(3-trifluoromethyl-phenyl)-1H-pyrazolo[4,3-c]isoquinoline,
3-methyl-5-(4-trifluoromethyl-phenyl)-1H-pyrazolo[4,3-c]isoquinoline,
1,3-dimethyl-5-(3-trifluoromethylphenyl)-1H-pyrazolo[4,3-c]-isoquinoline,
5-phenyl-3-trifluoromethyl-1H-pyrazolo[4,3-c]isoquinoline,
1,3-dimethyl-5-(3-trifluoromethylphenyl)-1H-pyrazolo[4,3-c]-isoquinoline,
1,3-dimethyl-5-(2,6-difluorophenyl)-1H-pyrazolo[4,3-c]-isoquinoline,
1-benzyl-5-cyclohexyl-3-methyl-1H-pyrazolo[4,3-c]-isoquinoline,
1-benzyl-5-naphthyl-3-methyl-1H-pyrazolo[4,3-c]-isoquinoline,
5-methoxymethyl-3-methyl-1H-pyrazolo[4,3-c]-isoquinoline,
7-methoxycarbonyl-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]-isoquinoline,

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7-methoxycarbonyl-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-isoquinoline,
7-dimethylamino-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]isoquinoline,
7-dimethylamino-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-isoquinoline,
6-dimethylamino-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]isoquinoline,
6-dimethylamino-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-isoquinoline,
8-dimethylamino-3-methyl-5-phenyl-1H-pyrazolo[4,3-c]isoquinoline,
8-dimethylamino-3-methyl-5-pyridin-2-yl-1H-pyrazolo[4,3-c]-isoquinoline,
1,3-dimethyl-5-(3-methyl-thiophen-2-yl)-1H-pyrazolo[4,3-c]-isoquinoline,
3-methyl-5-phenyl-9-trifluoromethyl-1H-pyrazolo[4,3-c]isoquinoline,
3-methyl-5-pyridin-2-yl-9-trifluoromethyl-1H-pyrazolo[4,3-c]-isoquinoline,
and
3-methyl-5-(2,3,4,5,6-pentafluoro-phenyl)-1H-pyrazolo[4,3-c]-isoquinoline.

17. (canceled)
18. (original) The method as claimed in claim 14, wherein the disease condition is selected from the group consisting of multiple sclerosis, atherosclerosis, inflammatory bowel disease, Alzheimer's disease, stroke and diabetes.
19. (original) The method as claimed in claim 18, wherein the disease condition is multiple sclerosis.
20. (original) The method as claimed in claim 18, wherein the disease condition is atherosclerosis.
21. (original) The method as claimed in claim 18, wherein the disease condition is inflammatory bowel disease.
22. (original) The method as claimed in claim 18, wherein the disease condition is Alzheimer's disease.

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23. (original) The method as claimed in claim 18, wherein the disease condition is stroke.

24. (original) The method as claimed in claim 18, wherein the disease condition is diabetes.